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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/665,658 | 09/19/2003 | Paula M. Jardieu | P1014R1C1D1C1 | 8846 |

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| EXAMINER | |
|---|---|
| HADDAD, MAHER M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | |

DATE MAILED: 03/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/665,658 | JARDIEU ET AL. | |
| | Examiner | Art Unit | |
| | Maher M. Haddad | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/19/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-7 are pending.

2. Applicant's election without traverse of Group 1, claims 1-7 drawn to a method of treating systemic lupus erythematosous comprising administering a humanized anti-CD11a antibody which binds specifically to human CD11a I-domain filed on 12/22/05, is acknowledged.

3. Claims 1-7 are under examination as they read on a method of treating systemic lupus erythematosous comprising administering a humanized anti-CD11a antibody which binds specifically to human CD11a I-domain.

4. The specification on page 1 should be amended to reflect the status of parent application No. 09/795,798.

5. Applicant's IDS, filed 9/19/03, is acknowledged.

6. Claim 1 is objected to for the following informalities: the word "erythmatosus" is misspelled. The correct spelling is erythematosus. Correction is required.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

*The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

8. Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not reasonably provide **enablement** for a method of treating systemic lupus erythematosus in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a humanized anti-CD11a antibody which binds specifically to human CD11a I-domain, said antibody containing a heavy chain variable region comprising the amino acid sequence of (a) CDR1 (SEQ ID NO: 10), CDR2 (SEQ ID NO: 11) and CDR3 (SEQ ID NO12 or (b) SEQ ID NO: 5, and a light chain variable region comprising the amino acid sequence of (a) CDR1 (SEQ ID NO:13), CDR2 (SEQ ID NO: 14) and CDR3 (SEQ IDNO15) or (b) SEQ ID NO: 2 in claim 1, wherein the humanized anti-CD11a antibody has all human Kappa I consensus light chain framework residues in claim 2, wherein the humanized anti-CD11a antibody has human VH subgroup III consensus heavy chain fraemork residue 93H in claim 3, wherein the humanized anti-CDH11a antibody has a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 5 and the light chain variable region compris9ng the amino acid sequence of SEQ I DNO:2 in claim 4, wherein the humanized anti-CD11a antibody is a full length antibody in calim 5, wherein in the humanized anti-CD11a antibody is a human IgG in claim 6, wherein the humanized anti-CD11a antibody is bound to a cytotoxic agent in claim 7. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification disclosure does not enable one skilled in the art to practice the invention with out an undue amount of experimentation. The specification fails to provide empirical data to show that method would work.

At issue is whether or not the claimed method would function to treat systemic Lupus erythematosous (SLE). The nature of the invention is such that it would require the administration of a humanized anti-CD11a antibody that would treat SLE. The specification discloses that that the humanized anti-CD11a antibody can be used to treat LFA-1-mediated disorders which include T cell inflammatory responses such as inflammatory skin diseases including autoimmune diseases such as systemic lupus erythematosus (SLE). No exemplification in the specification is drawn to the use of humanized anti-CD11a antibody to treat LFA-1 mediated disorders.

The skill in the art would doubt that the claimed method of treating systemic lupus erythematosous would work using humanized anti-CD11a antibody. Kevil *et al* (American Journal of Pathology, Vol. 165(2):609-616, 2004) suggested the therapeutic potential of LFA-1 inhibitors such as anti-LFA-1 antibodies for SLE. Kevil *et al* teach that loss of LFA-1 protects MRL/MpJ-Fas$^{lpr}$ mice from autoimmune disease. Further Kevil *et al* teach that mice deficient in LFA-1 showed significantly increased survival, decreased anti-DNA autoantibody formulation, and reduced glmerulonephritis. Kevil *et al* concludes that these studies identify LFA-1 as key contributor in the pathogenesis of autoimmune disease in this model, and further suggest that therapeutic strategies targeting this adhesion molecule may be beneficial for the treatment of SLE (see abstract). Importantly, Kevil *et al* teach that these data also show that loss of LFA-1 cannot completely inhibit autoantibody production and the development of autoimmunity in this lupus model (page 615, 2$^{nd}$ col., lines 1-3). Finally, Kevil *et al* teach that LFA-1 is a potential therapeutic target for SLE and that anti-LFA-1 antibodies may be useful for the treatment of SLE (see page 615, last full paragraph). However, Connolly *et al* (American Association of Immunologist, 1993) cast doubt that the anti-LFA-1 antibodies would work for the treatment of SLE using an animal model for SLE. Connolly *et al* teach that anti-LFA-1 treatment inhibits autoantibody production but does not prolong life in lupus-prone NZB/NZW mice (see abstract). The humanized anti-CD11a antibodies are designed to produce a desired therapeutic function that blocks LFA-1 interactions with its ligands with the goal of reversion of the disease process. Applicant's strategy to block LFA-1 interactions with its ICAM ligands in variety of immune disorders such as SLE using humanized anti-CD11a antibodies is fraught with inaccuracies and that these methods are still notably deficient in defining and describing the complexity of CD11a function in SLE.

The specification does not provide empirical data to show the efficacy of the humanized anti-CD11a antibodies on SLE. It is not clear that the skilled artisan could predict the efficacy of the humanized anti-CD11a on SLE, encompassed by the claims. It is unpredictable whether treating SLE with the humanized anti-CD11a antibody would reach a therapeutic end point. It is not

clear that the skilled artisan could predict the efficacy of the humanized anti-CD11a antibodies on SLE. The clinical value of such strategies has been show by Connolly et al to be ineffective for SLE.

Based on the absence of a specific and detailed description in Applicant's specification of how to effectively use the methods as claimed, and absence of working examples providing evidence which is reasonably predictive that the claimed methods are effective for treating SLE, and the lack of predictability in the art at the time the invention was made, an undue amount of experimentation would be required to practice the claimed methods with a reasonable expectation of success. There is no evidence of record that demonstrates that the humanized anti-CD11a antibodies can be use to treat SLE. The specification fails to provide working examples providing evidence which is reasonably predictive that the claimed methods are effective for the treatment of SLE. The lack of working examples is exacerbated because the invention is in a highly unpredictable art-the treatment of SLE- and while the level of skill of a practitioner in the art may be high, the state of the prior art is that it is in fact unknown and untested what are the underlying physiologic bases of the therapeutic effect of the humanized anti-CD11a antibodies, in the treatment of SLE.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

March 6, 2006

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Patent Examiner
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MAHER M. HADDAD
PATENT EXAMINER